**Advancing Strategies in Cardiopulmonary Disease: Pioneering Pathways to Therapeutic Innovation**

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Pulmonary arterial hypertension (PAH) remains a devastating condition marked by elevated pulmonary arterial pressure, progressive vascular remodelling, and persistent inflammation, ultimately leading to right ventricular failure. Despite decades of progress, current therapies primarily target vasoconstriction and offer symptomatic relief without halting disease progression. This gap underscores an urgent need for strategies that address the underlying biology of cardiopulmonary disease. Our work explores innovative therapeutic pathways that integrate vascular, inflammatory, and resolution biology. Using complementary ex vivo human lung models and in vivo disease systems, we reveal that PAH is characterised by disrupted pro-resolving signalling and sustained inflammatory activation, alongside structural changes in the pulmonary vasculature. Lipid mediator profiling and receptor analyses highlight resolution pathways as untapped targets for restoring vascular homeostasis. Novel agents tested in these models demonstrated effects beyond haemodynamic improvement—reducing vascular remodelling, modulating inflammatory gene expression, and preserving right ventricular function. These findings point toward a paradigm shift: therapies that combine vasodilation with anti-remodelling and immunomodulatory benefits, moving beyond symptom management to disease modification. By leveraging insights into resolution biology and vascular signalling, this research provides foundational knowledge for precision medicine in PAH and broader cardiopulmonary conditions. These strategies represent an innovative approach to improving patient outcomes and redefining therapeutic innovation in cardiovascular and pulmonary health.